

Determination of calprotectin levels in patients with cataract surgery

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Huseyin Erdal¹, Erdogan Yasar², Sibel Cigdem Tuncer³

¹ Department of Medical Genetics, Faculty of Medicine, Aksaray University, Aksaray

² Department of Ophthalmology, Afyonkarahisar Special Parkhayat Hospital, Afyonkarahisar

³ Department of Biochemistry, Faculty of Medicine, Aksaray University, Aksaray, Turkey

Abstract

Aim: The aim of the present study is to determine the calprotectin levels in patients with cataract surgery.

Material and Methods: This prospective study included 60 people, including 30 cataracts and 30 controls. Serum Calprotectin levels were determined in the ELx-800 (BioTek®) device using a commercial ELISA kit.

Results: Serum calprotectin levels in the cataract group were significantly higher than in the control group ($p=0.001$). Furthermore, we also found that calprotectin levels were significantly higher after cataract surgery than before cataract surgery ($p=0.01$). We found that Neutrophil-lymphocyte ratio (NLR) was higher, but no statistically significant difference was observed after cataract surgery compared to the controls ($p=0.07$).

Discussion: This study revealed that serum calprotectin levels can be used as a possible inflammation biomarker in the follow-up of inflammation caused by cataract surgery and also in the follow-up of cataract progression.

Keywords

Calprotectin, Cataract, Inflammation, Neutrophil-lymphocyte Ratio, Cataract Surgery

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Corresponding Author: Huseyin Erdal, Department of Medical Genetics, Faculty of Medicine, Aksaray University, Aksaray, Turkey.

E-mail: herdalyfa@gmail.com P: +90 543 414 08 15

Corresponding Author ORCID ID: <https://orcid.org/0000-0003-0786-5077>

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Introduction

Cataract surgical operation is one of the most common surgeries in the world. Cataract is the leading cause of reversible visual impairment and blindness, which is common in poor socioeconomic and developing countries [1,2]. Crystalline structures are the main proteins that make up the lens and lens surfaces, which are primarily responsible for the refractive function[1]. Changes in the sequence and character of crystalline proteins, such as precipitation, modification, and aggregation, are the main factors through which cataract formation occurs [3]. The only treatment for cataract is the surgical removal of the lens and its replacement with a permanent artificial intraocular lens (IOL) [4]. Successful cataract surgeries lead to a significant improvement in the patient's visual function and quality of life. It is widely accepted that surgical trauma to the ocular surface can induce an inflammatory response that includes the release of prostaglandins and the recruitment of neutrophils and macrophages. This process culminates in the production of chemical inflammatory mediators such as oxygen free radicals, proteolytic enzymes, and arachidonic acid cyclooxygenase and lipooxygenase metabolites, and leads to injection, flare-ups and peri-membrane cells are clinically detectable in the anterior compartment [5,6]. Increased reactive oxygen species (ROS) production is known to cause oxidative damage to the lens. The increase in intracellular oxidant levels damages various cell components and signaling pathways that affect many cellular processes related to aging and age-related diseases such as neurodegeneration and cataracts [7-10].

Calprotectin (CLP) is a 36 kDa protein and is a member of the S100 proteins, which is calcium modulated family [11,12]. CLP, an inflammation marker, consists mostly of neutrophils and accounts for approximately 60% of the cytosolic protein content in the neutrophil [13,14]. CLP is released from the body during filtration of inflamed tissue and shows the activity level of innate immunity [11]. Increased CLP levels have been demonstrated in various studies such as recurrent aphthous stomatitis [15], rheumatoid arthritis [13], bowel disease [16], various cancer types [17,18] and uveitis [19] during certain inflammatory conditions or infection. As far as we know, this is the first report to determine the serum calprotectin levels in patients undergoing cataract surgery.

Material and Methods

Study and control groups

A total of 30 patients who underwent cataract surgery were followed up at the Ophthalmology Department of Aksaray University Training and Research Hospital. The control group consisted of 30 healthy individuals with no statistically significant difference in terms of gender and age. Demographic information of the study and control groups was collected from the hospital automation system. Informed written consent was obtained from all patients. Patients with any systemic or autoimmune disease, history of active infection, and patients who had pseudoexfoliation, glaucoma, iridocyclitis, secondary malignancies with cataract, neurodegenerative diseases were excluded from the study. The present study was approved by the Aksaray University Clinical Research Ethics Committee (protocol number: 63-SBKA EK).

Sample collection of the study

Whole blood samples were collected from both the cataract patients and controls and centrifuged at 3600 rpm for 10 min. Subsequently, the obtained serum samples were taken into Eppendorf tubes and kept in a freezer at -80 C until the time of the experiment.

Measurement of calprotectin levels

We measured serum Calprotectin levels in the ELx-800 (BioTek®) device using a commercial ELISA kit (Elabscience Human Calprotectin ELISA Kit, catalog no: E-EL-H2357) and the values were expressed as nanograms per milliliter (ng / mL).

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) 22 (SPSS Inc., Chicago, IL, USA) program was used for statistical analysis. The normal distribution of the data was determined using the Shapiro-Wilk test. The mean differences between the two independent groups were compared with the Student's t-test. Comparison of values that did not fit the normal distribution was done with the Mann-Whitney U test. For abnormally distributed data, differences between more than two groups were compared with the Kruskal-Wallis analysis test. Comparison of parameters before and after cataract was performed with the Wilcoxon signed rank questionnaire in abnormally distributed data. The P-value < 0.05 was accepted as a statistical significance level.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

This study consisted of 60 people, including 30 cataracts and 30 control groups. There was no significant difference between the groups in terms of age and gender (Table 1).

Patients with Pseudoexfoliation, Glaucoma, Iridocyclitis, Cataract with secondary malignancy, Autoimmune diseases, Neurodegenerative diseases such as Alzheimer's and Parkinson's were excluded from the study.

In the Cataract group, 18 (60%) of the patients were male and 12 (40%) were female; In the control group, 15 (50%) of the participants were male and 15 (50%) were female. Among the laboratory parameters including C-reactive protein (CRP), White blood cell (WBC), Platelet-lymphocyte ratio (PLR) and Neutrophil- lymphocyte ratio (NLR) were not found to be significantly different between the groups (p>0.05). However, calprotectin levels were found significantly different between the groups (p<0.05) (Table 2). We also evaluated laboratory parameters before and after cataract surgery. C-reactive protein (CRP), White blood cell (WBC), Platelet-lymphocyte ratio (PLR) and Neutrophil- lymphocyte ratio (NLR) were not found to be significantly different between the groups (p>0.05). However, calprotectin levels were found significantly different between the groups (p<0.05) (Table 3).

Table 1. Demographic features of participants.

Parameter	Cataract (n=30) n %	Control (n=30) n %	p
Gender	Male 18 (60%)	15 (50%)	0.66*
	Female 12 (40%)	15 (50%)	
Age	66.1±7.32	65.4±6.71	0.68*

*: Chi-Square test, *: Student t –test.

Table 2. Comparison of laboratory parameters among groups.

Parameters	Before Cataract Surgery (n=30) (min-max)	After Cataract Surgery (n=30) (min-max)	Control (n=30) (min-max)	p*
C-reactive protein (CRP) mg/L	3.66 (0.95-9.51)	3.58 (0.83-11.9)	2.32 (1.45-4.9)	0.402
White blood cell (K/μl)	7.29 (4.32-11.45)	6.87 (3.67-9.85)	7.05 (4.3-9.2)	0.82
Calprotectin (median (range); ng/ml)	1.79 (0.99-3.21)	2.05 (1.36-2.75)	1.06 (0.56-3.06)	0.001
Platelet-lymphocyte ratio (PLR)	126.27 (49.3-236.6)	131.01 (47.3-209.3)	115.3 (26-161.3)	0.517
Neutrophil -lymphocyte ratio (NLR)	2.27 (0.89-6.37)	2.55 (1.08-4.90)	1.88 (1.20-2.54)	0.29
*Kruskal-Wallis analysis				

Table 3. Comparison of laboratory parameters before and after cataract surgery.

Parameters	Before Cataract Surgery (n=30) (min-max)	After Cataract Surgery (n=30) (min-max)	p [#]
C-reactive protein (CRP) mg/L	3.66 (0.95-9.51)	3.58 (0.83-11.9)	0.97
White blood cell (K/μl)	7.29 (4.32-11.45)	6.87 (3.67-9.85)	0.06
Calprotectin (median (range); ng/ml)	1.79 (0.99-3.21)	2.05 (1.36-2.75)	0.01
Platelet-lymphocyte ratio (PLR)	126.27 (49.3-236.6)	131.01 (47.3-209.3)	0.32
Neutrophil -lymphocyte ratio (NLR)	2.27 (0.89-6.37)	2.55 (1.08-4.90)	0.07
*Wilcoxon Signed Ranks Tests			

Discussion

In the present study, we demonstrated that serum calprotectin levels were significantly higher in patients with cataract compared to the controls (p=0.001) (Table1). In addition, we compare the PLR and NLR ratios of cataract and control groups and found no statistically significant difference. Moreover, we also evaluated calprotectin levels before and after surgery and it was found to be significantly higher in the post-cataract surgery group than in the pre-cataract surgery groups, p< 0.05 (Table 2). There was no statistically significant difference between CRP, WBC, PLR, NLR values before and after cataract surgery (p>0.005, Table 3). Both NLR and PLR ratios were higher in the post-cataract surgery group than in the pre-cataract surgery group, but they were not statistically significant (p>0.005, Table 3). CRP levels were not statistically significant before and after cataract surgery.

CLP is a complex protein belonging to the calcium-binding S100 family of proteins, mostly produced by neutrophils and monocytes [11,20]. CLP levels are clinically important, especially in inflammatory diseases and microbial infections. Calcium-binding proteins are known to be involved in intracellular signal transduction. It has been shown that calprotectin, which is an S100 protein family, plays an important role in myeloid cell metabolism [21]. When calprotectin leaves the cell, it performs an immunomodulatory function and plays a vital role in neutrophil defense. Therefore, myeloid appears to be an important regulatory protein in intracellular and extracellular inflammatory reactions. In studies conducted on various cancer types, a significant increase in serum calprotectin levels has been detected as a result of the inflammatory response, showing that this may be an important marker in the diagnosis of some cancer types. Topuz et al. reported that calprotectin levels in laryngeal cancer patients were higher compared to the benign laryngeal pathology to healthy control group. They hypothesized that it can be used as a marker in the diagnosis and follow-up of patients with laryngeal cancer [18].

In another study, Kayabası et al. reported that calprotectin levels were found to be significantly higher in the active lesion

group compared to the control group in a study performed on patients with recurrent aphthous stomatitis. They concluded that serum calprotectin levels can be used as a reliable and robust marker for recurrent aphthous stomatitis and active ulcer lesions [15]. Elsamea et al. showed that calprotectin levels were significantly higher in rheumatoid arthritis patients than that of osteoarthritis and controls. They assumed that high serum calprotectin levels were associated with disease activity, severity, and functional status [22]. In line with the previous studies, we found that calprotectin levels were significantly higher in patients with cataract in controls. We also evaluated serum calprotectin levels before and after cataract surgery and found them to be statistically significantly higher. We hypothesized that the determination of increased serum calprotectin levels can be used to assess the severity and follow-up of the disease. Studies have reported that NLR is a new biomarker that indicates the presence of inflammation. Özler and Akoğlu reported that they found NLR levels to be significantly higher in current aphthous stomatitis (RAS) patients compared to the control group [23]. Another study by Aza et al. showed that NLR levels were higher in breast cancer patients. They showed that NLR is an independent predictor of mortality in patients with cancer patients. In the present study, NLR levels in patients after cataract surgery were found to be higher than in control group, but it was not statistically significant. We concluded that calprotectin is a prominent biomarker than neutrophil-lymphocyte in terms of inflammatory response.

Conclusion

Calprotectin is a new diagnostic marker that can be used in the evaluation of patients with cataracts. Measurement of calprotectin levels may contribute to the follow-up of inflammation occurring during cataract surgery and also to monitoring the progression of cataracts.

Limitation of the study

The main limitation of the present study is the small sample size. Larger sample sizes are needed for further prospective studies.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

This study was approved by the Clinical Research Ethics Committee of Aksaray University (Date: 2022-04-07, No: 63-SBKA EK)

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of interest

The authors declare no conflict of interest.

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